abnormalities that are caused by the renin-angiotensin-aldosterone effects of the disorder from those that are not.

Standard renal function evaluation techniques that use either technetium Tc 99m pentetic acid (DTPA) (excreted by glomerular filtration) or iodohippurate sodium I 131 or I 123 (excreted primarily by tubular secretion) show a delayed transit time through the kidney and therefore a prolonged excretory phase that results from the renin effect of reducing urine flow on the affected side. When captopril is administered before these tests, there is a substantial drop in the glomerular filtration rate. This affects the ^{99m}Tc-DTPA renogram by dropping the rate of tracer accumulation and the iodohippurate renogram by delaying the transit time (time to peak) and excretion rate half-time owing to the altered dynamics. These changes are not noted in essential hypertension where there is either an increase or no significant change in the glomerular filtration rate. In patients with renovascular hypertension with severely reduced renal function, the magnitude of the change may be reduced, making the test less sensitive. In those with complete renal artery stenosis, although renin production is increased, there is no handling of these radiopharmaceuticals as is to be expected. In nearly complete stenosis, there is also no demonstrable captopril effect, but an iodohippurate study does show the classic retention pattern. In mild stenosis (<50%) there is neither increased renin production nor a captopril effect.

Although large-scale studies using captopril in this manner have not yet been done, the well-defined mechanistic response to angiotensin inhibition should significantly enhance the 80% to 85% sensitivity of standard renograms in identifying renovascular hypertension and differentiating it from essential hypertension and other renal diseases.

JOHN MAX VOGEL, MD
Sacramento, California

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Dacryoscintigraphy Revisited

NASOLACRIMAL DUCT OBSTRUCTION is a frequent cause of epiphora (excess tearing). A diagnostic evaluation is required to rule out other common causes of epiphora such as lower lid horizontal laxity or conjunctival inflammation. A proper diagnosis is essential because the traditional treatment of nasolacrimal duct obstruction is surgical correction. Recently a new technique has been described that uses a balloon catheter—like doing coronary angioplasty—to dilate the nasolacrimal duct. This has stimulated a renewed interest in a physiologic assessment of nasolacrimal duct patency.

Two office procedures may be done to evaluate nasolacrimal duct obstruction: irrigation of the lacrimal system and dye testing. Nasolacrimal duct obstruction may be diagnosed when there is complete obstruction to irrigation of the lacrimal system at the level of the nasolacrimal duct. In many patients with epiphora, however, there is no physiologic drainage of tears through the nasolacrimal duct, but forceful irrigation through the nasolacrimal duct may be accomplished (functional nasolacrimal duct obstruction). Functional nasolacrimal duct obstruction may be diagnosed by placing fluorescein dye in the eye and a cotton swab in the nose to recover the dye. This test has been criticized as unreliable because of problems recovering the dye in the nose of some patients.

The tearing process was first studied with radioisotopes in 1973. A major difference between a radionuclide dacryocystogram and an x-ray contrast dacryocystogram is that the radionuclide study is physiologic and better depicts the natural flow of tears. The study consists of placing a drop of technetium Tc 99m pertechnetate in the conjunctival space and imaging the passage of the labeled tears into the nose. X-ray dacryocystography, on the other hand, requires canalization of the nasolacrimal duct and the administration of contrast using pressure, which can mask the anomaly.

Recently 16 patients were studied before balloon dilatation of the nasolacrimal duct. In each case the dacryoscintigram showed the obstruction. In addition, the site of obstruction along the nasolacrimal path was found and the degree of obstruction was apparent. Dacryoscintigraphy is thus a useful diagnostic test to evaluate patients with epiphora and suspected functional nasolacrimal duct obstruction.

KENNETH P. LYONS, MD
BRUCE BECKER, MD
KENNETH ASHTON, MD
Long Beach, California

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Radiolabeled Monoclonal Antibodies for Detecting and Treating Cancer

THE USE OF MONOCLONAL ANTIBODIES offers a new procedure, called immunoscintigraphy, for detecting and treating cancer. The basic concept is to use monoclonal antibodies as a carrier to transport the radionuclide to the tumor sites, using the mechanism of the binding of antibody to the site of antigen. When antibodies are labeled with γ-ray-emitting radionuclides, such as technetium Tc 99m and others, they can be used to detect primary and metastatic lesions. The antibodies can also be labeled with β-ray-emitting radionuclides such as iodine 131 and others and be applied for treatment.

Radioimmunoscintigraphy is successfully used to detect solid tumors including melanoma; hepatocellular carcinoma; neuroblastoma; carcinomas of the breast, prostate, colorectum, lung, and ovary; and nonsolid tumors such as B-cell and T-cell lymphomas. In our experience, ^{99m}Tc-anti-melanoma antibody provides excellent quality diagnostic imaging with a high tumor-to-soft-tissue ratio. Besides the known lesions that have been identified, there are many unexpected lesions detected with this radiolabeled antibody and later confirmed to be metastatic melanoma lesions. Because of the need to alter treatment plans, the clinical importance of detecting unexpected sites cannot be overemphasized. This melanoma antibody is currently under the review of the Food and Drug Administration and is expected to be approved this year. Other antibodies such as those of lymphoma, breast cancer, lung cancer, colorectal, and prostate cancer are in the

early stages of investigation and available only in major medical centers.

The treatment of hepatocellular carcinoma, melanoma, neuroblastoma, B-cell and T-cell lymphomas, and ovarian carcinoma has been tried with varied but encouraging results. In one study about 50% of 105 patients with hepatocellular carcinoma responded to the treatment of ^{131}I-antiferritin antibody. Large doses (more than 200 mCi [7,400 MBq]) of ^{131}I-Lym-1 or anti-pan-B cell antibody were used to treat B-cell lymphoma with good responses in more than 30 patients.

The possible advantages of using monoclonal antibodies to detect and treat cancer are a binding of tumor-specific monoclonal antibody to the tumor site, providing high-intensity target to background images for tumor detection; a single imaging procedure and a single radiation exposure providing the information of disease in the whole body and eliminating the need for many procedures to stage the cancer; and giving a high radiation dose to tumor while sparing the normal tissue in the radioimmunotherapy.

There are several disadvantages in that only a small amount of injected labeled monoclonal antibody accumulates in the tumor. There is some nonspecific organ binding that varies with different antibodies and labeling methods. Also, all have a short shelf-life, which requires a fresh preparation.

Immunoscintigraphy and radioimmunotherapy may become an essential part of cancer staging and therapy for tumors such as melanoma, lymphoma, and carcinomas of the lung, breast, colon, and prostate.

DAVID C.P. CHEN, MD
MICHAEL E. SIEGEL, MD
Los Angeles

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Treatment of Bone Metastases

SKELETAL METASTASES are associated with a variety of cancers, being present in more than half of patients having breast or prostate cancer. These metastatic lesions can be extremely painful despite conventional forms of therapy such as chemotherapy, surgical excision, hormonal manipulation, or localized radiation therapy. The use of radionuclides in the treatment of bone metastases has been limited to that of phosphorus 32. Its use has not been widespread, however, owing to substantial hematologic side effects in patients receiving ^{32}P therapy.

Recently, patients with widespread skeletal metastases have been treated with strontium 89, rhenium 186, and samarium 153. These radionuclides are all β-ray emitters, with ^{186}Re and ^{153}Sm having the additional advantage of γ-ray emissions that also allow for imaging.

Because the largest clinical experience in Europe and the United States has been with the use of ^{89}Sr in the treatment of bone metastases, this radionuclide will be discussed in detail.

Strontium 89 is a pure β-ray emitter with the maximum energy of 1.5 MeV and an effective range in tissue of 0.8 cm. It has a half-life of 50.5 days and is produced by cyclotron. It is available as an aqueous solution of strontium Sr 89 chloride for intravenous injection. Strontium 89 was reported to be effective in relieving bone pain due to metastatic prostate cancer in 80% of patients and 89% of the patients having skeletal metastases due to breast cancer. This was achieved using a dose of 40 μCi (1.5 MBq) per kilogram given as a single intravenous injection. Pain relief lasted as long as six months after treatment, and retreatment at three-month intervals was possible without notable hematologic depression.

Because of the relative sparing of bone marrow by ^{89}Sr-chloride, which is a calcium analogue and not taken up directly by the bone marrow, about 20% of patients in one study showed no significant change in their leukocyte or total platelet count. The remaining 80% of the patients had an average 15% to 20% decrease in total platelets and leukocyte counts by the fifth week after ^{89}Sr-chloride was administered. A reduction in bone pain did not usually occur until 10 to 14 days after therapy, although a small percentage of patients did experience a flare phenomenon, with a significant increase in pain within 36 to 48 hours after ^{89}Sr therapy. Repeating the treatment is possible and well tolerated.

Although compounds containing ^{89}Sr, ^{186}Re, and ^{153}Sm are currently available only under investigational new drug protocols, they may be approved by the Food and Drug Administration for routine use in the near future. The use of all of the above radiopharmaceutical agents appears to have significant advantages over that of ^{32}P in the treatment of skeletal metastases, although a cure of the metastatic skeletal involvement is not possible with current dosage. Considerable palliation of pain and a better quality of life are attainable by using these therapeutic agents.

ROBERT F. CARRETTA, MD
Fair Oaks, California

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Radionuclide Synovectomy for Chronic Joint Effusion

THE USE OF INTRA-ARTICULARLY ADMINISTERED radiocolloid to selectively eradicate inflamed synovium was pioneered in Europe. Rather than actually surgically removing the synovium, the eventual desired outcome with this treatment is sclerosis of the synovium. Although encouraging results were initially reported in the 1960s using gold Au 198 colloid, this particular tracer had two potential drawbacks: the ^{198}Au had a γ-ray emission that added to the radiation exposure with little therapeutic value, and the particle size (0.02 μm) is small, yielding unacceptable leakage from the joint. More recently, radionuclides that do not emit γ-rays and are pure β-ray emitters have been used. The two most common are chromic phosphate P 32 and dysprosium 165 macroaggregates, which also have significantly larger particle size, thus minimizing leakage (approximately 750 μm and 5 μm, respectively).

The treatment is a simple outpatient procedure using an